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Detection of Small Changes in Psoriasis Intensity with PrecisePASI

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Key Words

Psoriasis severity · PASI · Psoriasis Area and Severity Index · PrecisePASI

Abstract

Background: The Psoriasis Area and Severity Index (PASI) is the score of choice to grade psoriasis severity and detect clinical changes. Due to low resolution based on the calculation of the score by fixed area classes, PASI scores <10 have little value. **Methods:** At 756 patient examinations, psoriasis activity was measured with both PASI and PrecisePASI. **Results:** PrecisePASI has a linear increase while PASI has a staircase pattern. Both scores meet at the endpoint-relevant values of body surface area (BSA) 10, 30, 50, 70 and 90%. PASI and PrecisePASI correlate significantly over the whole range of BSA. In the region of BSA <5%, PrecisePASI shows a significantly higher resolution ($p < 0.0001$). **Conclusion:** The calculation of PrecisePASI corrects the undesired inaccuracies of PASI in the lower BSA ranges and is a tool to use as an endpoint in trials aiming to detect differences in the lower ranges of BSA.

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Introduction

Since its original publication in 1978 [1], the Psoriasis Area and Severity Index (PASI) has become an important and irreplaceable tool for grading disease severity in psoriasis.

Nowadays it is used in most studies to measure treatment response. PASI has the drawback of being insensitive to milder changes, especially in the lower regions (PASI <10) [2]. This occurs because PASI uses a discontinuous score from 0 to 6 to grade area involvement rather than the actual percentages of area involvement (fig. 1). If the area of involvement changes within an area score interval, i.e. from 1% increasing to 9% which are both graded as area involvement of '1', the PASI remains unchanged due to its calculation.

In addition, the reproducibility of PASI has been criticized repeatedly [2–5] due to inter-observer variation, overestimation of the involved areas by untrained observers [6, 7] as well as its non-linear scale and lack of sensitivity at the lower end of its range [4].

However, as PASI is the gold standard of measurement of psoriasis disease activity, we did not seek to create a new score, but rather to improve sensitivity in the lower range of body surface area (BSA) by using a novel method of calculating the PASI score. PrecisePASI is calculated with the exact percentage of area involvement and may thus reflect small changes in surface involvement more accurately [8].

For milder psoriasis, PASI is rarely used and no single score of choice has been earmarked. To maintain compatibility with the wealth of earlier studies using PASI whilst improving precision in the range of BSA <10%, the validated clinical procedure of PASI measurement is applied with the actual percentage of area involvement instead of the imprecise area classes intervals [6, 9–11].

Table 1. Descriptive statistics and differences

BSA	PE	Mean PASI	SD	Min.	Max.	Mean PrecisePASI	SD	Min.	Max.	Mean of difference	95% CI	p value	p value summary
<2%	204	1.47	1.14	0.00	6.40	0.60	0.60	0.00	6.40	0.87	0.76 to 0.98	<0.0001	****
≥2% to <5%	192	2.65	1.24	0.20	6.80	2.29	1.09	0.20	5.60	0.37	0.28 to 0.46	<0.0001	****
≥5% to <10%	165	4.99	2.36	0.80	14.60	5.14	2.49	0.76	14.60	-0.14	-0.25 to -0.03	0.01	**
0–100%	756	5.23	6.47	0.00	59.40	5.24	7.11	0.00	60.50	-0.01	-0.09 to 0.07	0.79	n.s.

PE = Patient examinations; Min. = minimum; Max. = maximum.

Level of significance: n.s. = not significant; ** $p \leq 0.01$; **** $p \leq 0.0001$.

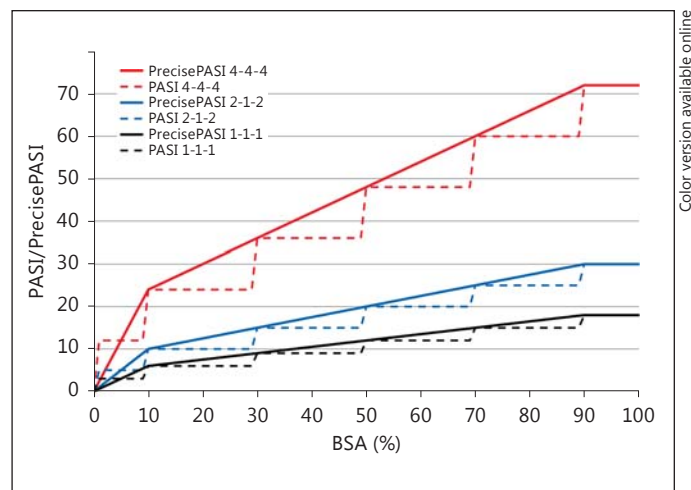


Fig. 1. Discontinuous increase in the area score in the normal PASI system versus the continuous increase in the PrecisePASI system for erythema, infiltration and desquamation of 1-1-1, 2-1-2 and 4-4-4 (staircase pattern and boundary points).

Methods

We collected PASI, PrecisePASI and BSA at 756 patient examinations in 328 different patients (222 male, 106 female, mean age \pm standard deviation [SD] 49.7 ± 15.4 years) during the time from May 2011 until February 2012. Patients with any kind of psoriasis affecting the skin and any kind of medication (topical, systemic or both) were included in the analysis. Non-plaque psoriasis cases were excluded. As the original PASI uses area classes (1: 0% to <10%; 2: $\geq 10\%$ to <30%; 3: $\geq 30\%$ to <50%; 4: $\geq 50\%$ to <70%; 5: $\geq 70\%$ to <90%; 6: $\geq 90\%$ to 100%; fig. 1), we integrated the percentage of affected BSA measured by patients' palm evaluation [12]. During the data collection, two dermatologists (A.A. Navarini, A.G.A. Kolios) independently measured both scores. Subsequently, a single consensus value was agreed upon and saved in the electronic patient registry. PrecisePASI was calculated using the same clinical criteria as PASI concerning erythema, scaling and infiltration, but instead of using area scores, the exact percentage of area involvement was utilized (fig. 2). The data were anonymized and analyzed with permission of the institutional review board.

Results

As shown in figure 1, PASI follows a 'staircase pattern' due to the area class and stays on a certain value until the next area class is reached although BSA is increasing. Instead, PrecisePASI scores increase linearly upon enlargement of area involvement while still overlapping with PASI at BSA 10, 30, 50, 70 and 90% (fig. 1). These points correspond to the lower thresholds of the six original PASI area classes [1].

Below a BSA of 5%, PASI scores tend to be higher than PrecisePASI measurements (see table 1 for descriptive statistics and differences). In the region of BSA <2%, PASI was up to a PASI value of 4.72 higher than PrecisePASI (mean of differences 0.87). With an increasing BSA of ≥ 2 to <5%, the difference decreased (mean of differences 0.37). In the region of BSA ≥ 5 to <10% instead, PASI was up to a PASI value of 5.42 lower than the calculation with actual percentages (mean of differences -0.14). Comparing PrecisePASI and PASI in the whole BSA range from 0 to 100%, 756 patient examinations were included, with a mean PrecisePASI of 5.23 (SD ± 6.47) and a mean PASI of 5.24 (SD ± 7.11) with a mean of the difference of -0.01 (95% confidence interval (CI) -0.09 to 0.07, $p = 0.79$, not significant), which was explainable due to reciprocal compensation with positive values in BSA ranges <5% and negative values in BSA ranges >5%. Hence over the whole range of BSA, PrecisePASI and PASI correlated significantly ($p < 0.0001$, Pearson correlation 0.9902, 95% CI 0.9887–0.9915) (fig. 3).

In 19 of 756 cases, the results of both scores were discordant around the threshold of 10, which can be relevant for therapeutic decisions. The distribution of results was analyzed in detail. In 18 patients PrecisePASI was between 10.1 and 13.41 (11.19 ± 0.79) while the corresponding PASI showed a value between 8.7 and 9.9 (9.27 ± 0.36), and in one patient PASI was at 10.1 and PrecisePASI at 9.88. For statistical analysis GraphPad Prism Ver-

0.1	*	(E _h + I _h + D _h)	*	IF(A _h < 10; A _h *0.2; IF(A _h > 89; 6; (A _h - 10)*0.05 + 2))	Head
+0.3	*	(E _t + I _t + D _t)	*	IF(A _t < 10; A _t *0.2; IF(A _t > 89; 6; (A _t - 10)*0.05 + 2))	Trunk
+0.2	*	(E _u + I _u + D _u)	*	IF(A _u < 10; A _u *0.2; IF(A _u > 89; 6; (A _u - 10)*0.05 + 2))	Upper extremity
+0.4	*	(E _l + I _l + D _l)	*	IF(A _l < 10; A _l *0.2; IF(A _l > 89; 6; (A _l - 10)*0.05 + 2))	Lower extremity
Area grading		Erythema Infiltration Desquamation		Exact area calculation: If BSA < 10% => factor 0.2 is added If BSA ≥ 10% => factor 0.05 is added IF(A > 89; 6; formula) means that when A > 89 is fulfilled, the result is 6, otherwise the formula is calculated	

Fig. 2. PrecisePASI formula.

sion 5 (GraphPad Software Inc., La Jolla, Calif., USA) was used. The paired double-sided t test was used for analysis of BSA, PASI and PrecisePASI and the Pearson test for correlation analysis.

Conclusion

PrecisePASI demonstrates an improved method to objectively measure and study mild psoriasis and its therapy in the lower BSA ranges. Several valid approaches to improve PASI have been published, though few are widely used and compatible with the original PASI [13–15]. In a systematic review by Puzenat et al. [4], PASI overall is rated as the gold standard concerning content validity and has good rates in internal consistency and intra-observer variation as well as acceptable rates in inter-observer variation and sensitivity to change. Compared to other scores, the PASI still satisfies the greatest number of validation criteria. The assessment of outcome measurements included the following key criteria: construct validity (Is the score able to study the disease?), content validity (Are the items of the score representative for the disease?), internal consistency (Are the various items of the score non-redundant?), intra-observer variation (Do two independent evaluations by the same observer give the same result?), inter-observer variation (Do two independent observers give the same score?), sensitivity to change (Can the score detect changes in the course of the disease?) and acceptability (Can the score be applied in routine practice/in clinical trials?) [4]. As PrecisePASI is a calculatory adaptation of PASI using identical clinical data, we assumed that the validity of PASI applied equally for both scores. During the data collection a consensus was made from two in-

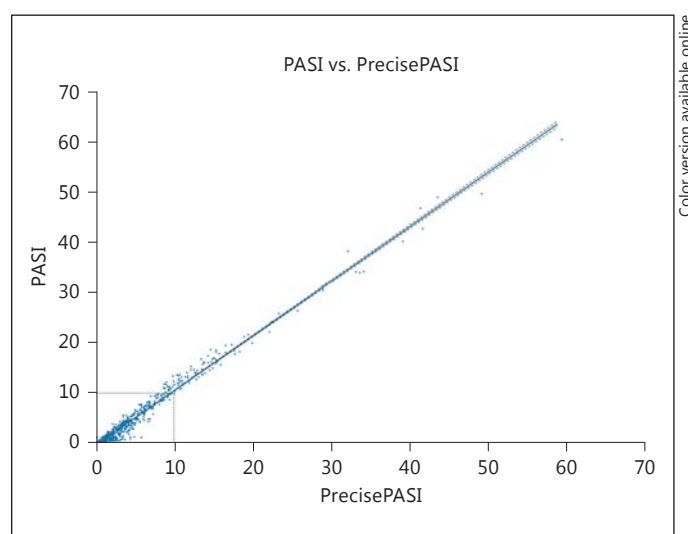


Fig. 3. Correlation of PASI and PrecisePASI ($p < 0.0001$, Pearson correlation 0.9902, 95% CI 0.9887–0.9915).

dependent analyses of two dermatologists. This method did not allow to gauge reproducibility and variability of PrecisePASI, which will be evaluated in subsequent studies.

PASI and PrecisePASI scores match closely at crucial points and correlate significantly over the whole range of BSA ($p < 0.0001$; table 1, fig. 3). Below a BSA of 5% PASI is higher than PrecisePASI, which could be interpreted as an overestimation of disease activity ($p < 0.0001$ for mean of difference), whereas in the region of BSA ≥ 5 to $< 10\%$ PASI is lower than PrecisePASI, which could be interpreted as underestimation of disease activity ($p = 0.01$ for mean of difference).

As nowadays patients with severe psoriasis are in general well-treated, we need an advanced but backward-compatible tool to gauge psoriasis activity in the lower ranges. The PrecisePASI method detects changes in the course of the disease in the lower BSA ranges. Thus, it is more sensitive in detecting change than PASI, a feature that may represent an advantage compared to the original PASI calculation.

Since the exact percentages of area involvement are recorded in PrecisePASI, it can be easily transformed to the normal PASI. In the online supplementary data (www.karger.com/doi/10.1159/000371811), a Microsoft Excel® sheet that we use at our clinic to simultaneously calculate both PASI scores is available for download (online suppl. table 1).

Treatment studies aiming to improve psoriasis in the lower PASI ranges may have difficulty demonstrating effects because the PASI score is relatively insensitive to detect improvements at BSA <10% (table 1). Using PrecisePASI, these limitations could be overcome. In addition, with a higher resolution in lower BSA ranges, PrecisePASI might also display more precisely the total im-

provement of moderate-to-severe psoriasis both in clinical care and trials. We propose that in future studies, especially with mild psoriasis, PrecisePASI be used as a secondary endpoint together with the normal PASI.

Author Contributions

A.A. Navarini and A.G.A. Kolios had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: A.A. Navarini. Acquisition of data: A.A. Navarini, A.G.A. Kolios. Analysis and interpretation of data: A.A. Navarini, L.E. French. Drafting of the manuscript: A.A. Navarini, A.G.A. Kolios. Critical revision of the manuscript for important intellectual content: A.A. Navarini, L.E. French. Statistical analysis: A.G.A. Kolios, A.A. Navarini. Obtained funding: L.E. French, A.A. Navarini. Administrative, technical or material support: A.A. Navarini, A.G.A. Kolios. Study supervision: A.A. Navarini.

Disclosure Statement

None of the authors has any financial interest or affiliations (relationships) to disclose. There was no funding or support.

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